UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte BARBARA L. HEMPSTEAD, ROSEMARY KRAEMER, SHAHIN RAFII, PHI WIEGAN and MICHAEL J. DONOVAN

Appeal No. 2006-0611
Application No. 09/830,520

HEARD: April 25, 2006

Before SCHEINER and ADAMS, Administrative Patent Judges.

Opinion by SCHEINER, Administrative Patent Judge.
Dissenting Opinion by MILLS, Administrative Patent Judge

DECISION ON APPEAL

This appeal involves claims to a method for inducing angiogenesis in a patient that has cardiac ischemia, and claims to a method of inducing angiogenesis in a patient that has a vascular disorder. The examiner has rejected claims 7, 9, 10, 18, 19, 55, 59 and 60, all the claims remaining in the application, as anticipated by the prior art. We have jurisdiction under 35 U.S.C. § 134. Because the cited references support a prima facie case of anticipation, which Appellant has not adequately rebutted, we affirm the rejection.

Background

"trk [(tropomyocin receptor kinase)] receptor ligands include brain derived neurotrophic factor ('BDNF'), NT-3, [and] NT-4" (Specification, page 11). "BDNF is a neurotrophin best characterized for its survival and differentiative effects on neurons expressing the trk B receptor kinase" (id.). "NT-3 is a member of the neurotrophin family . . . and mediates its action on trk C expressing neurons, and [has a] role in promoting the survival of subclasses of sensory and sympathetic neurons during the development of the peripheral nervous system" (id., page 12). "NT-4 is an activity dependent neurotrophic signal for growth and remodeling of adult motor neuron innervation" (id.).

In addition, according to appellants, "ectopic BDNF overexpression is associated with increased capillary density and increased survival of cardiac microvascular endothelial cells" (id.), "NT-3 promotes angiogenesis in a Matrigel assay" (id.), and NT-4 . . . promot[es] the formation of vascular networks in an in vivo Matrigel assay" (id., page 13). Accordingly, "[t]he present invention relates to a method of inducing angiogenesis which includes delivering a trk receptor ligand in an amount effective to induce angiogenesis" (id., page 11).

Discussion

The Claims

Claims 7, 9, 10, 18, 19, 55, 59 and 60 are pending and on appeal. Claims 18 and 19 depend from independent claim 7, while claims 10, 55, 59 and 60 depend, directly or indirectly, from independent claim 9. Appellants differentiate between claims 7 and 9 in their arguments (Appeal Brief, page 6), but do not present separate arguments for the dependent claims. Therefore, we will focus on claims 7 and 9 as

representative of the claimed invention. Claims 18 and 19 will stand or fall with claim 7, while claims 10, 55, 59 and 60 will stand or fall with claim 9. 37 CFR § 41.37(c)(1)(vii). Claims 7 and 9 read as follows:

> 7. A method for inducing angiogenesis in a patient that has cardiac ischemia, said method comprising: administering a trk receptor ligand to the patient in an amount effective to induce angiogenesis and to treat the cardiac ischemia, wherein said trk receptor ligand is selected from the group consisting of brain derived neurotrophic factor, NT-3 and NT-4.
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> 9. A method for inducing angiogenesis in a patient that has a vascular disorder, said method comprising: administering a trk receptor ligand to the patient in an amount effective to induce angiogenesis and to treat the vascular disorder, wherein said trk receptor ligand is selected from the group consisting of brain derived neurotrophic factor, NT-3 and NT-4.

According to the specification, "[c]ardiac ischemia includes cerebrovascular disorders caused by insufficient cerebral circulation" (id., page 17), while "non-cardiac vascular disorders include[ ] atherosclerosis, renal vascular disease, and stroke" (id.). "[F]or inducing angiogenesis and promoting vascular survival," the specification teaches that "delivering an effective amount of a trk receptor ligand includes delivering nanomolar concentrations of ligand to the target site" (id., pages 15-16). Finally, the specification teaches that "the trk receptor ligand can be administered in vivo orally, intravenously, intramuscularly, intraperitoneally, subcutaneously, [etc.]" (id., page 16).

Claim 7 is directed to a method of treating cardiac ischemia by administering BDNF, NT-3 or NT-4 to patient that has cardiac ischemia, in an amount effective to induce angiogenesis. Claim 9 is directed to a method of treating a vascular disorder by administering BDNF, NT-3 or NT-4 to patient that has a vascular disorder, in an amount effective to induce angiogenesis.

Anticipation

Claims 7, 9, 10, 18, 19, 55, 59 and 60 stand rejected under 35 U.S.C. § 102(e) over Alps.[1] Alps describes "intravenous administration of neurotrophic factors to treat or prevent neuronal damage resulting from ischemia, hypoxia or neurodegeneration" (Alps, column 4, lines 49-51). According to Alps, "bFGF, aFGF, CNTF, NGF, BDNF, NT3, IGF-I and IGF-II" (id., column 5, lines 9-10) "are suitable for the treatment of stroke or cardiac arrest which result[s] in ischemic or hypoxic damage or neurodegeneration" (id., column 4, lines 55-58). Alps explains that "[i]schemia is a deficiency of blood in a tissue, due to functional or actual obstruction of a blood vessel[ ] [which] may be caused by stroke or cardiac arrest" (id., column 6, lines 63-65). Finally, Alps teaches that an effective amount of the neurotrophic factor is "a dose of about 0.1 µg/kg body weight to 100 mg/kg" (id., column 5, lines 46-47).

The examiner reasons that even though Alps "do[es] not explicitly teach the induction of angiogenesis, the reference teaches the intravenous administration of BDNF, NT-3 or NT-4 . . . for the treatment of strokes and cardiac arrests, . . . [which] would inherently induce angiogenesis" (Examiner's Answer, page 3). "Furthermore," according to the examiner, "appellants have failed to clearly contrast the claimed patient population from those patients treated in the teachings of Alps" because "[a]ppellants do not distinguish strokes and cardiac arrests from . . . 'cardiac ischemia' or 'vascular disorder'" (id., page 5). Thus, "the current claims and the cited art teach administering the same compound to treat the same group of patients[,] [and] it does not appear that

[1] Alps et al., U.S. Patent No. 5,733,871, issued Mar 31, 1998.

. . . [there is] a manipulative difference in the method steps when compared to the prior art disclosure" (id., pages 5-6).

Appellants argue essentially that the claimed invention is a new use of BDNF, NT-3, and NT-4, which "were regarded as neurotrophic factors having no relevance to inducing angiogenesis" at the time of the invention (Brief, page 7; Madri Declaration, ¶ 9).[2] Appellants point out that "Alps relates to intravenous administration of pharmaceutically acceptable compositions of neurotrophic factors, such as bFGF, aFGF, NGF, CNTF, BDNF, NT3, NT4, IGF-I, and IGF-II, for treating or preventing neuronal damage as a consequence of ischemia, hypoxia, or neurodegeneration" (Brief, page 6), but "[t]he present invention . . . involves the discovery that BDNF, NT-3, and NT-4 can be used for the very different purpose of inducing angiogenesis" (id., page 7). According to appellants, "Alps' method of treating neuronal damage would not have suggested to scientists in the field that . . . [BDNF, NT-3, or NT-4] would be useful in inducing angiogenesis" (Brief, page 6; Madri Declaration, ¶ 4), therefore, Alps "cannot be anticipatory" (Brief, page 9).

While we agree with appellants that Alps teachings would not have suggested that BDNF, NT-3, and NT-4 would be useful in inducing angiogenesis, we do not agree that the present invention represents a new use for these compounds, as would be the case if the compounds were administered to a patient population that differed from the patient population described in Alps, or if the compounds were administered in a manner or amount ineffective to induce angiogenesis.

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[2] Declaration of Dr. Joseph A. Madri, submitted under the provisions of 37 CFR § 1.132, executed July 20, 2004.

That is not the case here. Alps describes "intravenous administration of neurotrophic factors . . . for the treatment of stroke or cardiac arrest which result[s] in ischemic or hypoxic damage" (Alps, column 4, lines 49-57), "in a dose of about 0.1 μm/kg body weight to 100 mg/kg" (id., column 5, lines 45-47). Stroke is explicitly mentioned as an example of a vascular disorder in the present specification (Specification, page 17, lines 20-21). In addition, the present specification indicates that "[c]ardiac ischemia includes cerebrovascular disorders caused by insufficient cerebral circulation" (id.), and Alps teaches that "[i]schemia is a deficiency of blood in a tissue, due to functional constriction or actual obstruction of a blood vessel . . . [which] may be caused by stroke or cardiac arrest" (Alps, column 6, lines 63-65). Thus, we find that Alps describes administration of neurotrophic factors to patients with a vascular disorder, and to patients with cardiac ischemia.

Alps teaches that "compositions [ ] suitable for the treatment of stroke or cardiac arrest" (Alps, column 4, lines 56-57) include bFGF, aFGF, NGF, CNTF, BDNF, NT3, NT4, IGF-I, and IGF-II (id., column 5, lines 9-10, and Abstract). We find that Alps specifically describes administering BDNF, NT-3 and NT-4 to patients, even though the reference largely focuses on bFGF. See e.g., Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1376, 77 USPQ2d 1321, 1326 (Fed. Cir. 2005) ("This court rejects the notion that one of these [fourteen] ingredients cannot anticipate because it appears without special emphasis in a longer list.").

Alps further teaches intravenous administration of the neurotrophic factors "in a dose of about 0.1 μm/kg body weight to 100 mg/kg" (id., column 5, lines 45-47). According to the present specification, "the trk receptor ligand can be administered [ ]

orally, intravenously, [etc.]" (Specification, page 16). The present specification does not appear to contain an express statement regarding an amount of BDNF, NT-3 or NT-4 effective to induce angiogenesis, other than an assertion that "delivering an effective amount of a trk receptor ligand includes delivering nanomolar concentrations of ligand to the target site" (id., pages 15-16). Nevertheless, appellants do not dispute that the dosages described by Alps would be sufficient to induce angiogenesis. Thus, we find that Alps describes administering BDNF, NT-3 and NT-4 in a manner and amount inherently effective to induce angiogenesis.

Finally, we agree with the examiner that the fact that Alps' working examples "use[ ] focal or global ischemia models to induce neuronal damage" and involve "neither the claimed pool of patients (i.e., patients having cardiac ischemia or having a vascular disorder), [nor] the claimed trk receptor ligands" (Brief, page 10; Madri Declaration, ¶ 6), is irrelevant in this context. Appellants offer no authority, and we know of none, that supports the proposition that the teachings of the prior art are limited to working examples and/or preferred examples.

Therefore, we find, as does the examiner, that Alps describes administering BDNF, NT-3 and NT-4 to the same patient populations required by claims 7 and 9, in a manner and amount effective to induce angiogenesis. That being the case, "the discovery that BDNF, NT-3, and NT-4 can be used for the very different purpose of inducing angiogenesis" (Brief, page 7), "corresponds to a claimed new benefit or characteristic of an invention otherwise in the prior art[,]" and it is well settled that "the new realization alone does not render the old invention patentable." Perricone v. Medicis Pharm. Corp., 432 F.3d 1368, 1377, 77 USPQ2d 1321, 1327 (Fed. Cir. 2005).

"[A] limitation or the entire invention is inherent and in the public domain if it is the 'natural result flowing from' the explicit disclosure of the prior art." Id. (citations omitted).

The facts of Perricone are very similar to the facts of the instant case, and illustrate the difference between claims that recite a new use of an old composition, and claims that recite a newly recognized benefit of an old method. Perricone involved two sets of claims, one directed to preventing sunburn damage, and the other to treatment of skin sunburn. In each case, the claims required topical application of a fatty acid ester of ascorbic acid. The prior art described topical application of the same compound (among thirteen others) to skin, in an amount that encompassed the claimed effective amount. The court found that the claims directed to preventing sunburn damage to exposed skin surfaces were anticipated by the prior art, even though the prior art "[did] not disclose any benefit directed to skin sunburn, or any other specific skin disorders, as claimed" (id. at 1376, 77 USPQ2d at 1326). On the other hand, the court found that the claims directed to treating skin sunburn were directed to a new use of the prior art compounds, and therefore not anticipated, because the prior art "[did] not disclose topical application to skin sunburn" (id. at 1379, 77 USPQ2d at 1328). That is, the prior art did not disclose applying the compound to the same population (people with sunburn) as required by the claims. As the court explained, "[t]he issue is not . . . whether [the prior art] lotion if applied to skin sunburn would inherently treat that damage, but whether [the prior art] discloses the application of its composition to skin sunburn" (id. at 1378, 77 USPQ2d at 1328).

As summarized in Perricone, id. at 1375-76, 77 USPQ2d at 1325-26 (Fed. Cir. 2005):

> A single prior art reference that discloses, either expressly or inherently, each limitation of a claim invalidates that claim by anticipation. Minn. Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc., 976 F.2d 1559, 1565 [24 USPQ2d 1321] (Fed. Cir. 1992). Thus, a prior art reference without express reference to a claim limitation may nonetheless anticipate by inherency. See In re Cruciferous Sprout Litig., 301 F.3d 1343, 1349 [64 USPQ2d 1202] (Fed. Cir. 2002). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claims limitations, it anticipates." Id. (quoting MEHL/Biophile Int'l Corp. v. Milgraum, 192 F.3d 1362, 1365 [52 USPQ2d 1303] (Fed. Cir. 1999). Moreover, "[I]nherency is not necessarily coterminous with knowledge of those of ordinary skill in the art. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art." Id.; see also Schering Corp. v. Geneva Pharms., 339 F.3d 1373, 1377 [67 USPQ2d 1664] (Fed. Cir. 2003) (rejecting the contention that inherent anticipation requires recognition in the prior art) (citing In re Cruciferous Sprout Litig., 301 F.3d at 1351; MEHL/Biophile, 192 F.3d at 1366).

"Thus, when considering a prior art method, the anticipation doctrine examines the natural and inherent results in that method without regard to the full recognition of those benefits or characteristics within the art field at the time of the prior art disclosure." Id. at 1378, 77 USPQ2d at 1327. Based on our determination that Alps describes administering BDNF, NT-3 and NT-4 to a patient with cardiac ischemia or a vascular disorder, in a manner and amount effective to induce angiogenesis, we conclude that the examiner has set forth a prima facie case of anticipation.

The dissent would interpret the present claims to require that the method be practiced with the intent to induce angiogenesis, based largely on the holdings in Rapoport v. Dement, 254 F.3d 1053, 59 USPQ2d 1215 (Fed. Cir. 2001) and Jansen v.

Rexall Sundown Inc., 342 F.3d 1329, 68 USPQ2d 1154 (Fed. Cir. 2003). We do not agree that these cases support that proposition.

In Rapoport, the court considered whether claims to a method of treating sleep apnea with buspirone was anticipated by a disclosure of treating anxiety secondary to sleep apnea with the same agent. The court interpreted the claims to be limited to treating the underlying disorder itself, based in part on the application's statement that the drug should be administered "at the hour of sleep." Id. at 1060, 59 USPQ2d at 1220. The allegedly anticipating reference did not specify that the drug should be administered at bedtime, see id. at 1062, 59 USPQ2d at 1221, and therefore the evidence did not show that carrying out the prior art method would inherently result in treating sleep apnea.

Jansen involved claims drawn to "methods of 'treating or preventing macrocytic-megaloblastic anemia' by administering a combination of folic acid and vitamin B12 'to a human in need thereof.'" Id. at 1330, 68 USPQ2d at 1155. As in Perricone, the court's decision turned on whether the alleged infringer (Rexall) administered the combination to the same population required by the claims – humans in need of treatment or prevention of macrocytic-megaloblastic anemia. The court found that it did not, and found no infringement.

Finally, to the extent that the dissent focuses on the prosecution history of the Alps patent, we do not agree that an enablement rejection in that case is relevant here.

Again, based on our determination that Alps describes administering BDNF, NT-3 and NT-4 to a patient with cardiac ischemia or a vascular disorder, in a manner and amount effective to induce angiogenesis, we conclude that the examiner has set

forth a prima facie case that Alps anticipates claims 7 and 9. Moreover, appellants have not provided any evidence that the compounds and amounts thereof described in Alps do not inherently induce angiogenesis. Therefore, we affirm the § 102 rejection of claims 7 and 9 over Alps. Claims 18 and 19 fall with claim 7, and claims 10, 55, 59 and 60 fall with claim 9.

Time Period for Response

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Toni R. Scheiner)
Administrative Patent Judge)
) BOARD OF PATENT
)
Donald E. Adams) APPEALS AND
)
Administrative Patent Judge) INTERFERENCES
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Judge MILLS, respectfully dissenting.

I would reverse the rejection of the claims for anticipation in view of Alps.

The standard under § 102 is one of strict identity. "Under 35 U.S.C. § 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim." Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997). "Every element of the claimed invention must be literally present, arranged as in the claim." Richardson v. Suzuki Motor Co., Ltd., 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

In my view, Alps does not specifically disclose a method of inducing angiogenesis, as claimed. The method of claim 7 requires administration of a trk receptor ligand to the patient in an amount effective to induce angiogenesis and to treat the cardiac ischemia, wherein said trk receptor ligand is selected from the group consisting of brain derived neurotrophic factor, NT-3 and NT-4. The specific examples of Alps describes the administration of bFGF and NGF in a focal ischemia model of cerebral artery occlusion in mice or rats. There is no specific example administering the claimed trk inhibitors, brain derived neurotrophic factor, NT-3 and NT-4 to a patient having cardiac ischemia, stroke or to induce angiogenesis. Thus, Alps does not literally describes every element of the claimed invention, arranged as in claim 7, and does not anticipate.

While the majority seemingly acknowledges (page 5) that Alps would not have suggested that BDNF, NT-3, and NT-4 would be useful in inducing angiogenesis, the corollary is not acknowledged, i.e., if Alps does not provide a specific example of inducing angiogenesis by administering any of BDNF, NT-3, and NT-4, then Alps does

not provide a specific example of administration of BDNF, NT-3, and NT-4 for any purpose, more particularly, for the treatment of cardiac ischemia or stroke.

1. a) Appellants have proffered the Declaration under 37 CFR § 1.132 of Joseph A. Madri to show that one of ordinary skill in the art reading the disclosure of Alps would not have understood at the time the application was filed that all neurotrophins were recognized to possess the ability to induce angiogenesis. In this regard, the declarant acknowledges that Alps states that "[s]ome neurotrophic factors are also capable of promoting neurite outgrowth and glial cell and blood vessel restoration or inducing cells to secrete other neurotrophic factors." Declaration, page 2, paragraph 8. However, according to the Declarant, Alps makes clear that with regard to promoting blood vessel formation, Alps is talking only about bFGF." Id. Dr. Madri concludes that, "I, like others skilled in the area of angiogenesis, reading Alps would not have regarded it as teaching BDNF, NT-3, or NT-4 would be useful in inducing angiogenesis." Declaration, page 3, paragraph 8.

In support of this position taken by the Declarant, appellants' Evidence Appendix includes Exhibits B.-E. (already of record in the application) that describe the properties of neurotrophins which are trk receptor ligands and "no way suggests that trk receptor ligands are useful in promoting angiogenesis." Brief, page 8. In my view, this evidence also rebuts the examiner's prima facie case of anticipation and refutes the general statement in Alps that, at the time of filing, each of the neurotrophins listed in Alps were recognized to possess the property of blood vessel restoration.

b. The Federal Circuit, has in several cases, indicated that the preamble of a claim to a method with a stated objective should be interpreted to require that the method be practiced with the intent to achieve the objective stated in the preamble. For example, in Jansen v. Rexall Sundown Inc., 342 F.3d 1329, 68 USPQ2d 1154 (Fed. Cir. 2003), the claim at issue was directed to

> A method of treating or preventing macrocytic-megaloblastic anemia in humans which anemia is caused by either folic acid deficiency or by vitamin B-12 deficiency which comprises administering a daily oral dosage of viatamin preparation to a human in need thereof comprising at least about 0.5 mg. of vitamin B12 at least about 0.5 mg. of folic acid.

In Jansen, the alleged contributory infringer, Rexall, sold an over-the-counter dietary supplement that contains folic acid and vitamin B12 in the claimed amounts. The Federal Circuit concluded in Jansen, that the claims in Jansen are properly interpreted to mean that the combination of vitamins must be administered to a human with a recognized need to treat or prevent macrocytic-megaloblastic anemia. Jansen, 342 F.3d at 1334, 68 USPQ2d at 1158. The Federal Circuit in Jansen also referenced a similar issue which arose in Rapoport v. Dement, 254 F.3d 1053, 59 USPQ2d 1215 (Fed. Cir. 2001).

> A similar issue arose in *Rapoport*, an interference proceeding before the PTO's Board of Patent Appeals and Interferences. The count in that case read as follows:
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> A method *for treatment of sleep apneas* comprising administration of a therapeutically effective amount of a Formula I azapirone compound or a pharmaceutically effective acid addition salt thereof *to a patient in need of such treatment* . . . 254 F.3d at 1056 (emphases added). On appeal we gave weight to the ordinary meaning of the preamble phrase "for treatment of sleep apneas," interpreting it to refer to sleep apnea, *per se*, not just "symptoms associated with sleep apnea." *Id.* at 1059. Rapoport argued that the count was unpatentable on the ground that a prior art reference disclosed that a form of the compound recited in the

> claim could be administered, not for treatment of sleep apnea itself, but for treatment of anxiety and breathing difficulty, a symptom of apnea. *Id.* at 1061. We rejected that argument, stating, **"There is no disclosure [in the[prior art reference that the compound] is administered to patients suffering from sleep apnea *with the intent to cure the underlying condition.*" *Id.*** (emphasis added). Thus, the claim was interpreted to require that the method be practiced with the intent to achieve the objective stated in the preamble.

Jansen, 342 F.3d at 1333, 68 USPQ2d at 1157.

In another relevant case, Perricone v. Medicis Pharmaceutical Corp., 432 F.3d 1368, 1376, 77 USPQ2d 1321, 1326 (Fed. Cir. 2005), the claims were directed to a method of treating or preventing sunburn by the topical application of vitamin C in fat soluble form. The alleged anticipatory reference, Pereira, disclosed a cosmetic composition for topical application, including skin benefit ingredients, and all the various ingredients in the concentrations claimed. The District Court concluded that Pereira anticipates because the topical application of his composition would inherently yield Perricone's benefits. Id., at 1326. Perricone argued that Pereira does not disclose any benefit directed to skin sunburn. Id. The Federal Circuit concluded that, "Pereira is silent about any sunburn prevention or treatment benefits . . ." Id., at 1328. Thus, no infringement by the Rexall vitamin supplement was found.

In the present case, the claim is directed to a method for inducing angiogenesis in a patient having a vascular disorder. Alps allegedly discloses a select group of neurotrophic factors for the treatment of neuronal damage in the central nervous system of individuals in need of such treatment. Abstract. Evidence of record submitted by appellants shows that one of ordinary skill in the art would not have understood Alps to disclose that any or all trk inhibitors have the ability to induce angiogenesis, with any

reference to angiogenesis induction in Alps limited to bFGF. This evidence is unrebutted by the examiner.

Like Jansen, there is no disclosure in Alps of the administration of trk inhibitors for the indicated purpose of inducing angiogenesis. Alps allegedly suggests that neurotrophins, in general, may be useful in treating neuronal damage of the central nervous system, such as in stroke patients, but provides no specific example of administration of any of the claimed compounds to a stroke patient or patient having cardiac ischemia or other vascular disorder. "[I]n some unpredictable areas of chemistry and biology, there is no conception until the invention has been reduced to practice." MacMillan v. Moffett, 432 F.2d 1237, 1234-40, 167 USPQ 550, 552-553 (CCPA 1970). In the present case, there has been no reduction to practice or provision of a specific example of administration of the claimed compounds. If the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties. See, e.g., In re May, 574 F.2d 1082, 1094, 197 USPQ 601, 611 (CCPA 1978). The unpredictability of the biological arts also supports a finding of lack of anticipation in the present case.

c. Appellants and the Declarant allege that one of ordinary skill in the art would not have understood Alps to described the use of the claimed trk inhibitors to treat angiogenesis. This position of appellant is tantamount to arguing that Alps does not provide an enabling disclosure of inducing angiogenesis with trk inhibitors, and thus cannot be 35 U.S.C. § 102 prior art to the method of the pending claims.

A review of the prosecution history of the Alps patent would appear to support and affirm this position taken by appellants, that one of ordinary skill in the art would not have understood that trk inhibitors in general, as claimed would have been useful in promoting angiogenesis, as they are not enabled. The original claims in Alps were directed to the treatment of neuronal damage in the central nervous system comprising a neurotrophic factor with dependent claims to bFGF,aFGF,CNTF, BDNF, NGF, NT3, NTF4, IGF-I, and IGF-II. The examiner entered a rejection of the claims for lack of enablement, arguing "applicants themselves admit that pharmokinetic factors such as the stability of the protein in the body, half-life, absorption efficiency, binding affinity for target cells and biotransformation have not been considered yet are important considerations for the efficacy, and the enablement of the claimed subject matter." Alps, Paper No. 10 dated April 9, 1996, pages 3-4. The examiner of the Alps application also argues that "[n]o guidance has been given as to dosages, routes of administration or pharmaceutical formulations to direct on skilled in the art how to use the claimed peptides, either alone or in combination in human patients." Paper No. 10, page 4. In Alps, the patentee conceded to the examiner's rejection of the claims for lack of enablement, and amended the claims to recite a method of preventing cell death due to focal ischemia by administering bFGF intravenously. Alps, Paper No. 12. See also, Alps, Claim 1.

"In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'. . . ." In re Hoeksema, 399 F.2d

269, 158 USPQ 596 (CCPA 1968). See Manual of Patent Examining Procedures (MPEP) § 2121.01 [R-3]. The disclosure in an assertedly anticipating reference must provide an enabling disclosure of the desired subject matter; mere naming or description of the subject matter is insufficient, if it cannot be produced without undue experimentation. Elan Pharm., Inc. v. Mayo Found. For Med. Educ. & Research, 346 F.3d 1051, 1054, 68 USPQ2d 1373, 1376 (Fed. Cir. 2003) (At issue in Elan was whether a prior art reference enabled one of ordinary skill in the art to produce Elan's claimed transgenic mouse without undue experimentation. Without a disclosure enabling one skilled in the art to produce a transgenic mouse without undue experimentation, the reference would not be applicable as prior art.). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." In re Donohue, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985).

Prior art under § 102(b) must sufficiently describe a claimed invention to have placed the public in possession of that invention. In re Donohue, 766 F.2d 531, 533 [226 USPQ 619] (Fed. Cir. 1985); In re Samour, 571 F.2d 559, 562 [197 USPQ 1] (CCPA 1978). The proper test qualifying a publication as a §102(b) bar is "whether one skilled in the art to which the invention pertains could take the description of the invention in the printed publication and combine it with his own knowledge of the particular art and from this combination be put in possession of the invention on which a patent is sought." In re LeGrice, 301 F.2d 929, 939, 133 USPQ 365, 379 (CCPA 1962).

The Declaration under 37 CFR § 1.132 of Joseph A. Madri reasonably evidences that one of ordinary skill in the art reading the disclosure of Alps would not have understood at the time the application was filed that all neurotrophins were recognized to possess the ability to induce angiogenesis. Thus the disclosure of Alps, taken with one of ordinary skill in the art's own knowledge would not have put one of ordinary skill in the art in possession of the invention. Thus, Alps does not provide an enabling disclosure and is not 102 prior art to the claimed method.

One must be able to make the claimed invention without undue experimentation. In re Elsner, 381 F.3d 1125, 72 USPQ2d 1038 (Fed. Cir. 2004). See also, Gould v. Quigg, 822 F.2d 1074, 1077, 3 USPQ2d 1302,1303 (Fed. Cir. 1987) (ultimate issue of enablement is one of law based on underlying factual findings). Moreover, as is the case with most issues arising under 35 U.S.C., and particularly 35 U.S.C. 112, ... each case must be decided on its own facts. Ex parte Tanksley, 26 USPQ2d 1384, 1387 (Bd. Pat. App. & Int. 1991); In re Wyer, 655 F.2d 221, 210 USPQ 790 (CCPA 1981); In re Steele, 305 F.2d 859, 134 USPQ 292 (CCPA 1962). Compare, In re Durden, 763 F.2d 1406, 1410, 226 USPQ 359, 361 (Fed. Cir. 1985). In re Mayne, 104 F.3d 1339, 1341, 41 USPQ2d 1451, 1453 (Fed. Cir. 1997). In this case, the facts do not support a prima facie case of anticipation under 35 U.S.C. § 102.

d. In my view, the applicability of the legal principles such as those set forth in In re Schaumann, 572 F.2d 312, 197 USPQ 5 (CCPA 1978), to the present case is in apt. In Schaumann, claims to a specific compound were anticipated because the prior art taught a generic formula embracing a limited number of compounds closely related to each other in structure and the properties possessed by the compound class of the

prior art was that disclosed for the claimed compound. In Schaumann the facts substantiated that one of ordinary skill in the art would "at once envisage the subject matter within the reference." 572 F.2d at 312, 197 USPQ at 5 (CCPA 1978).

That is not the case here. In the present case, the disclosure of the alleged § 102 prior art, Alps, lists, albeit, a smaller number of compounds, six different neurotrophic factors. The evidence provided by Appellants in the Brief indicates that the naming of a compound as a neurotrophin does not necessarily imply the compounds are structural homologs, or that one of ordinary skill in the art would have expected that they share the same or similar structure or function. According to Chao[3], page 586, first paragraph, (a review article of record), neurotrophic factors "are capable of promoting survival and differentiation of sensory neurons, but they display markedly different activities in other cell populations." Moreover, there is significant level of unpredictability as to how these compounds behave in vivo, i.e., as to how these compounds are used. For example, "neurotrophins interact with two major classes of receptors. The major singal-transducing receptors are a family of three membrane spanning tyrosine kinases named trkA, trkB, trkC . . . NGF interacts selectively with trkA, whereas brain-derived neurotrophic factor and neurotrophin 4/5 interact primarily with trkB. Neurotrophin 3 activates trkB and to a lesser extent, trkC. Neurotrophins also bind to a receptor called $p75^{NTR}$. It has been "strongly argued that the cellular setting is important for neurotrophin action." Chao, page 588, column 2. In addition, the FGF family modulates proliferation of cells derived from the mesoderm and neuroectoderm, but also promotes

[3] Chao et al. (Chao), "Neurotrophin Receptors: A Window into Neuronal Differentiation, Neuron, Vol. 9, pp. 583-593 (1992)

differentiation of hippocampal, cerebellar and ciliary neurons." Although NGF and FGF exert their effects through tyrosine phosphorylation, the initial events stimulated by these factors are distinctive . . ." Id.

The present facts, in my view, are no different from appeals we receive for patent applications claiming a thousand DNA or amino acid sequences which have been found to possesses a portion of the sequence in common. In those cases, computer analysis has indicated that the sequences share a common, and often minimal similarity with a known sequence, however the function of the thousand different sequences has yet to be determined. See also, In re Fisher, 421 F.3d 1365, 76 USPQ2d 1255 (Fed. Cir. 2005). In many instances we have found claims to these sequences in those appeals to lack both utility, and an enabling disclosure as to how to use the sequences, even though the application disclosure summarily lists that they are useful for the treatment of over 100 types of cancer. At the same time, with 18 month publication of patent applications, these disclosures are available as potential § 102 prior art to later filed sequences filed with sufficient enabling disclosures and clear utilities. Such patent application disclosures as in our previous appeals, must be analyzed on their facts for all they teach one of ordinary skill in the art, and scrutinized to determine whether they are supported by an enabling disclosure, instead of being found per se to represent §102 prior art and to possess an enabling disclosure for the uses indicated therein. These facts may well be a harbinger of fact scenarios to come.

Likewise, in the present case, the disclosure of the alleged § 102 prior art, Alps, lists, albeit, a smaller number of compounds, six different neurotrophic factors. However, in my view, Alps is not supported by an enabling disclosure and thus does not

anticipate the method of use of the pending claims before us. In fact, in the Alps prosecution, the examiner did not even find the specific neuronal damage prevention uses for the specifically disclosed neurotrophins to be supported by an enabling disclosure. The patentee's claims in Alps were limited to use bFGF only for the prevention of neuronal damage.

e. In my view, wrote application of case law such as Schaumann to the present facts is not appropriate, especially in view of Appellants' unrebutted Declaration and publication evidence, that one of ordinary skill in the art would not have recognized the disclosed neurotrophins to possess angiogenic properties.

f. Another issue relevant as to whether Alps represents an anticipation of the claimed subject matter, is that the examiner, in my view, has not provided a clear indication that the broad dosage range of neurotrophic factor disclosed in Alps and the claimed effective amount are the same or similar. Alps describes administering neurotrophic factor in a dose of 0.1 µg/kg body weight to 100mg/kg to prevent neuronal damage. Column 5, lines 45-49. Again, while the examiner of the Alps patent may have found this dosage range to be potentially relevant to the administration of bFGF to prevent neuronal damage or promote angiogenesis in a patient having a vascular disorder, the examiner of the Alps patent did not find the dosage disclosure of Alps to be enabling for use of other neurotrophic factors listed in the Alps disclosure for the treatment of stroke or cardiac ischemia. Appellants' example 14 shows administration of 50-100 ng/ml of rhBDNF, rhNT-4, or rhNT-3. The record does not reflect that the examiner has made a showing or comparison of the prior art amounts and the claimed amounts, or indicated that they are the same or substantially the same.

g. The Supreme Court long ago explained that "if an old device or process be put to a new use which is not analogous to the old one, and the adaptation of such process to the new use is of such a character as to require the exercise of inventive skill to produce it, such new use will not be denied the merit of patentability." [Emphasis added.] Ansonia Brass & Copper Co. v. Elec. Supply Co., 144 U.S. 11, 18, 12 S.Ct. 601, 36 L.Ed. 327 (1892). Such a case is before us here.

In view of the above legal precedent, based on the present record, I would reverse the rejection under 35 U.S.C. §102 of claims 9, 10, 55 and 59-60 over Alps.

2. The examiner's attention is also directed to a possible additional relevant publication to the pending claims. Upon return of the application to the examiner, it is recommended that the examiner consider the disclosure of Donovan et al., "Neurotrophin and neurotrophin receptors in vascular smooth muscle cells. Regulation of expression in response to Injury," American Journal of Pathology, Vol. 147, pp. 309-324 (1995). This prior art publication appears to conclude that BDNF, NT-3, NT-4, and the trkB and C receptors present in atherosclerotic lesions, and suggests that neurotrophins play an important role in regulating the response of vascular smooth

muscle cells to injury, promoting vascular smooth muscle cell migration. The examiner should consider the relevance of this publication to the pending claims and whether an obviousness rejection over Alps in view of Donovan would be appropriate.

Demetra J. Mills
Administrative Patent Judge

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